Amendment, claims 31-34 have been canceled as being drawn to the non-elected invention; claim 21 has been canceled; claims 16, 19, and 20 have been amended; and claims 36-38 have been added. Thus, claims 16-20, 22-30, and 35-38 are pending.

Claim 16 has been amended to incorporate the subject matter of claim 21, which has been canceled. Claims 19 and 20 have been amended in response to the restriction requirement to delete recitation of non-elected SEQ ID NOs: 1-6, 11-14, 19, and 20.

Claims 36-38 have been added to secure enhanced protection for Applicants' invention. Claim 36 is supported, for example, in the specification at page 15, lines 21-31. Claim 37 is supported, for example, in Example 6 of the specification. Claim 38 is supported, for example, in the specification at page 16, lines 4-15. No new matter is added.

Rejection/Election

The Office Action acknowledged Applicants' election of Group I (claims 16-30 and 35) and SEQ ID NOs:9 and 10, with traverse. In the present Amendment, Applicants have amended the claims to recite SEQ ID NOs:9 and 10, the elected polynucleotide and polypeptide sequences. The amended claims are also directed to SEQ ID NOs:7 and 8 (Momordica charantia) and SEQ ID NOs:15 and 16 (Glycine max). Applicants respectfully request that, in addition to examining the application with respect to the elected species of SEQ ID NOs:9 and 10, that the Examiner further consider the claims as presently amended.

Applicants' Background of the Invention section of the specification provides a background of the protein disulfide isomerase (PDI) family. In many of the articles mentioned in the specification and cited in the Information Disclosure Statement filed September 8, 2000 (see, specifically, Kim and Mayfield, McKay et al., Mazzarella et al., Shorrosh and Dixon, Wong and Bateman, and Kajino et al., all of record), the characteristics of PDI polypeptides are discussed. These characteristics include two conserved active site domains that regulate the formation, reduction, and isomerization of disulfide bonds involved in protein folding. These domains have the conserved amino acid sequence Tryp-Cys-Gly-His-Cys. In the RB60s, of which SEQ ID NO:10 is an example, there is also an endoplasmic reticulum retaining signal (Lys-Asp-Glu-Leu). As can be seen in Appendix A, SEQ ID NO:9 encodes a polypeptide of 570 amino acids that includes a start methionine and a stop codon. The amino acid sequence of SEQ ID NO:10, encoded by SEQ ID NO:9, has all three elements considered to be present in all RB60s. The first WCGHC domain corresponds to amino acids 114 through 118, the second WCGHC domain corresponds to amino acids 459 through 463, and the ER retention signal is at amino acids 567 through 570. Similarly, the amino acid sequences of SEQ ID NOs: 8 and 16, which are full-length balsam pear and soybean disulfide isomerase polypeptides, include these elements. Applicants believe that it would not be an undue burden on the Patent Office's resources to examine SEQ ID NOs:7, 8, 15, and 16, in tandem with the elected sequences of SEQ ID NOs:9 and 10.

Claim Rejections under 35 U.S.C. § 112, first paragraph

Claims 16-30 and 35 were rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. That rejection is respectfully traversed.

Applicants submit that the subject matter of claims 16-30 and 35 is described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The disclosure provides full-length protein disulfide isomerases in SEQ ID NOs:8, 10, and 16. In addition, the specification demonstrates percent identity of SEQ ID NOs:8, 10, and 16 to known protein disulfide isomerases, indicates that known protein disulfide isomerase characteristics are present in SEQ ID NOs:8, 10, and 16, and the literature provides assays for measuring protein disulfide isomerase activity (see, Kajino et al., Biosci. Biotechnol. Biochem. 58(8), pp. 1424-1429 at page 1425, last paragraph before Results). Applicants submit that the specification provides the requisite written description of the claimed subject matter.

Claims 16-30 and 35 were also rejected as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. That rejection is respectfully traversed.

At the outset, Applicants note that the claims (specifically, independent claim 16) are directed to isolated polynucleotides encoding polypeptides comprising an amino acid sequence that is at least 85% identity to Applicants' SEQ ID NOs:8, 10, or 16, rather than polypeptides comprising at least 85% homology with protein disulfide isomerases from *Humicola insolens* or *Bos taurus* as recited in the Office Action sentence spanning pages 5 and 6.

Claim 16 recites two physiochemical properties of the claimed polynucleotides. Specifically, this claim recites (1) a specific sequence identity and (2) a function limitation (i.e., enzymatic activity). One of skill in the art could determine, without undue experimentation, whether a polynucleotide falls within the scope of claim 16 by simply comparing the amino acid sequence encoded by this polynucleotide with the amino acid sequence of the SEQ ID NO: recited in claim 16, and by transforming cells with an expression cassette containing the polynucleotide and assaying the transformed cells for enzymatic activity.

Specifically, Example 7 of the specification describes the construction of an expression cassette, and assays for measuring protein disulfide isomerase activity are known to those skilled in the art. Applicants have also provided conserved active domains that regulate the formation, reduction, and isomerization of disulfide bonds involved in protein

folding. Although these tasks may be time consuming, they do not defeat patentability. As stated in MPEP §2164.06:

> "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." In re Colianni, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977)." "'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

Thus, because the tasks noted above are routine, and because the specification provides a reasonable amount of guidance, these tasks do not require undue experimentation. The claims therefore are fully enabled.

Conclusion

In view of the amendments and remarks above, Applicants respectfully submit that the application is in condition for allowance. The Examiner is invited to contact the undersigned if there are any questions concerning the prosecution of this application.

The Commissioner is authorized to charge Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company) for any requisite fees due or to credit any overpayment.

Respectfully submitted,

PAUL D. GOLIAN
ATTORNEY FOR APPLICANTS
REGISTRATION NO. 42,591
TELEPHONE: 302-992-3749
FACSIMILE: 302-892-1026

Dated: September 21, 2001

VERSION WITH MARKING TO SHOW CHANGES MADE

In showing the changes, deleted material is shown in brackets and stricken through, and inserted material is shown underlined.

In the Claims:

16. (Amended) An isolated polynucleotide comprising:

(a) a nucleotide sequence encoding [~~that encodes~~] a [~~protein~~] polypeptide having disulfide isomerase[~~, the polypeptide having a sequence identity of at least 85% based on the Clustal method of alignment, when compared to a polypeptide selected from the group consisting of SEQ ID NOs:2, 4, 6, 8, 10, 12, 14, 16, 18, and 20~~] activity, wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO:8, 10, or 16 have at least 85% identity, or

(b) the complement of the nucleotide sequence, wherein the complement and the nucleotide sequence contain the same number of nucleotides and are 100% complementary.

19. (Amended) The polynucleotide of Claim 16 wherein the polynucleotide encodes a polypeptide selected from the group consisting of SEQ ID NOs:[~~2, 4, 6,~~] 8, 10, [~~12, 14,~~] and 16[~~, 18, and 20~~].

20. (Amended) The polynucleotide of Claim 16[,] wherein the polynucleotide comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs:[~~1, 3, 5,~~] 7, 9, [~~11, 13,~~] and 15[~~, 17, and 19~~].

21. (Canceled)

31. (Canceled)

32. (Canceled)

33. (Canceled)

34. (Canceled)

36. (Added) A vector comprising the polynucleotide of Claim 16.

37. (Added) A seed comprising the chimeric gene of Claim 22.

38. (Added) A method for isolating a polypeptide encoded by the polynucleotide of Claim 16 comprising isolating the polypeptide from a cell transformed with said polynucleotide.

Appendix A

Translation of the nucleotide sequence in SEQ ID NO:9 and alignment with the nucleotide sequence in SEQ ID NO:10.

```
        1 ---------+---------+---------+---------+---------+---------+-61
SEQ  9    CTCACCAGCTGCCCGCGCATCCAATTCCTCTCGCTGGACGGCTGCAGCACATCATCAGGTG
           SerProAlaAlaArgAlaSerAsnSerSerArgTrpThrAlaAlaAlaHisHisGlnVal  -

       62 --------+---------+---------+---------+---------+---------+- 121
SEQ  9    AGACCGTGAGAGGGAATGGGATCAACAACAATGTCCCCTCCATCTTTTCCCGTCGTCCTC
           ArgProEndGluGlyMetGlySerThrThrMetSerProProSerPheProValValLeu  -
SEQ 10                    MetGlySerThrThrMetSerProProSerPheProValValLeu  -

      122 --------+---------+---------+---------+---------+---------+- 181
SEQ  9    CTGCTCCTCCTCCTCGCCACCATAGCCGCAGCCGCCGGAAGCAACATGGATGAGGAGGTG
          LeuLeuLeuLeuLeuAlaThrIleAlaAlaAlaAlaGlySerAsnMetAspGluGluVal  -
SEQ 10    LeuLeuLeuLeuLeuAlaThrIleAlaAlaAlaAlaGlySerAsnMetAspGluGluVal  -

      182 --------+---------+---------+---------+---------+---------+- 241
SEQ  9    GTGGACGACCTCCAGTATCTTATTGACAACTCCGACGACATCCCCACCAACGATCCCGAC
          ValAspAspLeuGlnTyrLeuIleAspAsnSerAspAspIleProThrAsnAspProAsp  -
SEQ 10    ValAspAspLeuGlnTyrLeuIleAspAsnSerAspAspIleProThrAsnAspProAsp  -

      242 --------+---------+---------+---------+---------+---------+- 301
SEQ  9    GGGTGGCCTGAGGGAGACTACGACGACGACGACCTTCTCTTCCAAGATCAGGACCAGGAC
          GlyTrpProGluGlyAspTyrAspAspAspAspLeuLeuPheGlnAspGlnAspGlnAsp  -
SEQ 10    GlyTrpProGluGlyAspTyrAspAspAspAspLeuLeuPheGlnAspGlnAspGlnAsp  -

      302 --------+---------+---------+---------+---------+---------+- 361
SEQ  9    CTCACAGGCCACCAGCCGGAGATCGACGAGACCCACGTAGTGGTCCTCGCCGCCGCAAAC
          LeuThrGlyHisGlnProGluIleAspGluThrHisValValValLeuAlaAlaAlaAsn  -
SEQ 10    LeuThrGlyHisGlnProGluIleAspGluThrHisValValValLeuAlaAlaAlaAsn  -

      362 --------+---------+---------+---------+---------+---------+- 421
SEQ  9    TTTTCCTCCTTCCTCGCCTCCAGCCACCATGTTATGGTTGAGTTCTACGCACCTTGGTGT
          PheSerSerPheLeuAlaSerSerHisHisValMetValGluPheTyrAlaProTrpCys  -
SEQ 10    PheSerSerPheLeuAlaSerSerHisHisValMetValGluPheTyrAlaProTrpCys  -

      422 --------+---------+---------+---------+---------+---------+- 481
SEQ  9    GGCCACTGCCAGGAGCTCGCCCCGGGATTAAGCCGGCGCCGCGCGCATCTCGCCGGCTCA
          GlyHisCysGlnGluLeuAlaProGlyLeuSerArgArgArgAlaHisLeuAlaGlySer  -
SEQ 10    GlyHisCysGlnGluLeuAlaProGlyLeuSerArgArgArgAlaHisLeuAlaGlySer  -
```

```
     482 --------+---------+---------+---------+---------+---------+- 541
SEQ  9   ACCAACCAACCAAGGCCCAACTTCGCCCTTGCCAAGGTCGACGCCACCGAGGAAACCGAC
         ThrAsnGlnProArgProAsnPheAlaLeuAlaLysValAspAlaThrGluGluThrAsp  -
SEQ 10   ThrAsnGlnProArgProAsnPheAlaLeuAlaLysValAspAlaThrGluGluThrAsp  -

     542 --------+---------+---------+---------+---------+---------+- 601
SEQ  9   CTCGCCCAGAAGTACGACGTCCAGGGCTTCCCCACCATCCTCTTCTTCATCGATGGCGTC
         LeuAlaGlnLysTyrAspValGlnGlyPheProThrIleLeuPhePheIleAspGlyVal  -
SEQ 10   LeuAlaGlnLysTyrAspValGlnGlyPheProThrIleLeuPhePheIleAspGlyVal  -

     602 --------+---------+---------+---------+---------+---------+- 661
SEQ  9   CCCAGAGGCTATAACGGAGCCAGGACCAAGGAAGCCATCGTCGACTGGATCAACAAGAAG
         ProArgGlyTyrAsnGlyAlaArgThrLysGluAlaIleValAspTrpIleAsnLysLys  -
SEQ 10   ProArgGlyTyrAsnGlyAlaArgThrLysGluAlaIleValAspTrpIleAsnLysLys  -

     662 --------+---------+---------+---------+---------+---------+- 721
SEQ  9   CTCGGCCCAGCCGTGCAAAATGTCACCAGCGTCGACGAGGCCCAGAGCATACTCACCGGA
         LeuGlyProAlaValGlnAsnValThrSerValAspGluAlaGlnSerIleLeuThrGly  -
SEQ 10   LeuGlyProAlaValGlnAsnValThrSerValAspGluAlaGlnSerIleLeuThrGly  -

     722 --------+---------+---------+---------+---------+---------+- 781
SEQ  9   GATGACAAAGCCGTCCTTGCCTTCCTCGACACACTATCCGGTGCTCACAGTGATGAGCTT
         AspAspLysAlaValLeuAlaPheLeuAspThrLeuSerGlyAlaHisSerAspGluLeu  -
SEQ 10   AspAspLysAlaValLeuAlaPheLeuAspThrLeuSerGlyAlaHisSerAspGluLeu  -

     782 --------+---------+---------+---------+---------+---------+- 841
SEQ  9   GCTGCTGCTTCGAGGCTGGAAGATAGCATCAACTTTTATCAGACTTCGACTCCTGATGTT
         AlaAlaAlaSerArgLeuGluAspSerIleAsnPheTyrGlnThrSerThrProAspVal  -
SEQ 10   AlaAlaAlaSerArgLeuGluAspSerIleAsnPheTyrGlnThrSerThrProAspVal  -

     842 --------+---------+---------+---------+---------+---------+- 901
SEQ  9   GCTAAGCTTTTCCATATCGATGCAGCAGCGAAGCGTCCATCCGTAGTGCTGCTGAAGAAA
         AlaLysLeuPheHisIleAspAlaAlaAlaLysArgProSerValValLeuLeuLysLys  -
SEQ 10   AlaLysLeuPheHisIleAspAlaAlaAlaLysArgProSerValValLeuLeuLysLys  -

     902 --------+---------+---------+---------+---------+---------+- 961
SEQ  9   GAGGAGGAGAAGTTGACCTTCTATGATGGGGAGTTTAAAGCATCAGCCATTGCTGGTTTT
         GluGluGluLysLeuThrPheTyrAspGlyGluPheLysAlaSerAlaIleAlaGlyPhe  -
SEQ 10   GluGluGluLysLeuThrPheTyrAspGlyGluPheLysAlaSerAlaIleAlaGlyPhe  -

     962 --------+---------+---------+---------+---------+---------+- 1021
SEQ  9   GTGTCTGCTAACAAGCTTCCTTTGGTGACCACACTAACTCAAGAAACTTCCCCTTCTATT
         ValSerAlaAsnLysLeuProLeuValThrThrLeuThrGlnGluThrSerProSerIle  -
SEQ 10   ValSerAlaAsnLysLeuProLeuValThrThrLeuThrGlnGluThrSerProSerIle  -
```

```
    1022 --------+---------+---------+---------+---------+---------+- 1081
SEQ  9   TTTGGCAATCCAATCAAGAAGCAGATTTTACTATTTGCTGTTGCAAGCGAGTCCACCAAA
         PheGlyAsnProIleLysLysGlnIleLeuLeuPheAlaValAlaSerGluSerThrLys  -
SEQ 10   PheGlyAsnProIleLysLysGlnIleLeuLeuPheAlaValAlaSerGluSerThrLys  -

    1082 --------+---------+---------+---------+---------+---------+- 1141
SEQ  9   TTTCTGCCCATCTTTAAGGAAGCAGCAAAACCATTTAAGGGAAAGTTATTATTTGTCTTT
         PheLeuProIlePheLysGluAlaAlaLysProPheLysGlyLysLeuLeuPheValPhe  -
SEQ 10   PheLeuProIlePheLysGluAlaAlaLysProPheLysGlyLysLeuLeuPheValPhe  -

    1142 --------+---------+---------+---------+---------+---------+- 1201
SEQ  9   GTGGAACGAGACAGTGAGGAAGTTGGTGAACCAGTTGCCGACTACTTTGGTATTACTGGA
         ValGluArgAspSerGluGluValGlyGluProValAlaAspTyrPheGlyIleThrGly  -
SEQ 10   ValGluArgAspSerGluGluValGlyGluProValAlaAspTyrPheGlyIleThrGly  -

    1202 --------+---------+---------+---------+---------+---------+- 1261
SEQ  9   CAAGAGACCACAGTTCTTGCTTACACTGGTAATGAAGATGCTAGGAAATTTTTTCTTGAT
         GlnGluThrThrValLeuAlaTyrThrGlyAsnGluAspAlaArgLysPhePheLeuAsp  -
SEQ 10   GlnGluThrThrValLeuAlaTyrThrGlyAsnGluAspAlaArgLysPhePheLeuAsp  -

    1262 --------+---------+---------+---------+---------+---------+- 1321
SEQ  9   GGTGAGGTGTCACTTGAAGCTATAAAGGACTTCGCTGAAGGTTTCTTGGAAGACAAGCTT
         GlyGluValSerLeuGluAlaIleLysAspPheAlaGluGlyPheLeuGluAspLysLeu  -
SEQ 10   GlyGluValSerLeuGluAlaIleLysAspPheAlaGluGlyPheLeuGluAspLysLeu  -

    1322 --------+---------+---------+---------+---------+---------+- 1381
SEQ  9   ACACCATTCTACAAATCGGAACCAGTGCCTGAATCTAATGATGGGGATGTGAAAATTGTT
         ThrProPheTyrLysSerGluProValProGluSerAsnAspGlyAspValLysIleVal  -
SEQ 10   ThrProPheTyrLysSerGluProValProGluSerAsnAspGlyAspValLysIleVal  -

    1382 --------+---------+---------+---------+---------+---------+- 1441
SEQ  9   GTTGGGAAGAATCTGGATCTAATAGTTTTTGATGAAACAAAAGATGTACTTCTTGAGATA
         ValGlyLysAsnLeuAspLeuIleValPheAspGluThrLysAspValLeuLeuGluIle  -
SEQ 10   ValGlyLysAsnLeuAspLeuIleValPheAspGluThrLysAspValLeuLeuGluIle  -

    1442 --------+---------+---------+---------+---------+---------+- 1501
SEQ  9   TATGCACCATGGTGTGGTCATTGTCAATCGCTGGAACCTACTTACAACAATCTAGCCAAG
         TyrAlaProTrpCysGlyHisCysGlnSerLeuGluProThrTyrAsnAsnLeuAlaLys  -
SEQ 10   TyrAlaProTrpCysGlyHisCysGlnSerLeuGluProThrTyrAsnAsnLeuAlaLys  -

    1502 --------+---------+---------+---------+---------+---------+- 1561
SEQ  9   CATCTACGTAGTGTTGACTCCCTTGTGGTAGCCAAAATGGATGGTACTACCAATGAGCAT
         HisLeuArgSerValAspSerLeuValValAlaLysMetAspGlyThrThrAsnGluHis  -
SEQ 10   HisLeuArgSerValAspSerLeuValValAlaLysMetAspGlyThrThrAsnGluHis  -
```

```
    1562 --------+---------+---------+---------+---------+---------+- 1621
SEQ  9   CCACGTGCAAAGTCTGACGGATACCCGACGATTCTCTTCTATCCAGCTGGGAAGAAAAGC
         ProArgAlaLysSerAspGlyTyrProThrIleLeuPheTyrProAlaGlyLysLysSer  -
SEQ 10   ProArgAlaLysSerAspGlyTyrProThrIleLeuPheTyrProAlaGlyLysLysSer  -

    1622 --------+---------+---------+---------+---------+---------+ 1681
SEQ  9   TTTGAGCCAATCACTTTTGAGGGGGAGCGGACAGTGGTAGATCTGTACAAGTTCATCAA
         PheGluProIleThrPheGluGlyGluArgThrValValAspLeuTyrLysPheIleLys  -
SEQ 10   PheGluProIleThrPheGluGlyGluArgThrValValAspLeuTyrLysPheIleLys  -

    1682 ---------+---------+---------+---------+---------+---------+- 1741
SEQ  9   GAAACATGCTAGCATCCCTTTCAAGTTGAAGCGCCAGGAGTCGAGAACCGAGAGCACTCGG
         LysHisAlaSerIleProPheLysLeuLysArgGlnGluSerArgThrGluSerThrArg  -
SEQ 10   LysHisAlaSerIleProPheLysLeuLysArgGlnGluSerArgThrGluSerThrArg  -

    1742 --------+---------+---------+---------+---------+---------+- 1801
SEQ  9   GCGGAGGGTGTGAAGAGCTCTGGTACGAACTCAAAGGACGAACTGTAAAGAGCTCAGGGT
         AlaGluGlyValLysSerSerGlyThrAsnSerLysAspGluLeuEndArgAlaGlnGly  -
SEQ 10   AlaGluGlyValLysSerSerGlyThrAsnSerLysAspGluLeu-

    1802 --------+---------+---------+---------+---------+---------+- 1861
SEQ  9   TGGATGTGTGTTGGAGTGGATCAGGGTGAAAGTTTCCATCTCAATACAAGTAGATCGATC
         TrpMetCysValGlyValAspGlnGlyGluSerPheHisLeuAsnThrSerArgSerIle  -
          -

    1862 --------+---------+---------+---------+---------+---------+- 1921
SEQ  9   TTGGTGGATGCGAGTGCAGTGTTGGCCTGAGGGAGGAGCAGCAGAGATGAGTGCTTACTG
         LeuValAspAlaSerAlaValLeuAlaEndGlyArgSerSerArgAspGluCysLeuLeu  -
        -

    1922 --------+---------+---------+---------+---------+--- 1973
SEQ  9   CTTAGAGAGAGGAATGAAATCAGCAACTAATCAAATAAAATCAAATTCCATT
         LeuArgGluArgAsnGluIleSerAsnEndSerAsnLysIleLysPheHis    -
          -
```